

**THE EMBODIMENTS OF THE INVENTION IN WHICH AN EXCLUSIVE  
PROPERTY OR PRIVILEGE IS CLAIMED ARE DEFINED AS FOLLOWS:**

1. A method of treating malignant mesothelioma in an animal comprising administering to said animal an effective amount of an antisense oligonucleotide of 7 to about 100 nucleotides in length, said antisense oligonucleotide comprising a sequence of at least 7 consecutive nucleotides complementary to a thymidylate synthase mRNA.
2. The method according to claim 1, wherein said thymidylate synthase mRNA is a human thymidylate synthase mRNA.
3. The method according to claim 2, wherein said antisense oligonucleotide comprises at least 7 consecutive nucleotides of the sequence as set forth in SEQ ID NO:1.
4. The method according to claim 1, wherein said antisense oligonucleotide comprises one or more phosphorothioate internucleotide linkages.
5. The method according to claim 1, wherein said antisense oligonucleotide comprises one or more 2'-O-methoxyethoxy modified sugars.
6. The method according to claim 1, wherein said malignant mesothelioma is pleural mesothelioma.
7. The method according to claim 1, wherein said mesothelioma is drug resistant.
8. The method according to claim 1, wherein said animal is a human.
9. A method of treating malignant mesothelioma in an animal comprising administering to said animal an effective amount of an antisense oligonucleotide of 7 to about 100 nucleotides in length in combination with one or more chemotherapeutic agents, said antisense oligonucleotide comprising a sequence of at least 7 consecutive nucleotides complementary to a thymidylate synthase mRNA.

10. The method according to claim 9, wherein said one or more chemotherapeutic agent is selected from the group of: doxorubicin, epirubicin, mitomycin, cyclophosphamide, ifosfamide, cisplatin, carboplatin, 5-FU, 5-FUdR, raltitrexed and pemetrexed, or a combination thereof.
11. The method according to claim 9, wherein said thymidylate synthase mRNA is a human thymidylate synthase mRNA.
12. The method according to claim 11, wherein said antisense oligonucleotide comprises at least 7 consecutive nucleotides of the sequence as set forth in SEQ ID NO:1.
13. The method according to claim 9, wherein said antisense oligonucleotide comprises one or more phosphorothioate internucleotide linkages.
14. The method according to claim 9, wherein said antisense oligonucleotide comprises one or more 2'-O-methoxyethoxy modified sugars.
15. The method according to claim 9, wherein said malignant mesothelioma is pleural mesothelioma.
16. The method according to claim 9, wherein said mesothelioma is drug resistant.
17. The method according to claim 9, wherein said animal is a human.
18. A method of enhancing the cytotoxicity of a chemotherapeutic agent against neoplastic cells comprising the step of contacting said cells with an effective amount of an antisense oligonucleotide of 7 to about 100 nucleotides in length and a chemotherapeutic agent, said antisense oligonucleotide comprising at least 7 consecutive nucleotides complementary to a thymidylate synthase mRNA.
19. The method according to claim 18, wherein said chemotherapeutic agent is selected from the group of: 5-FU, 5-FUdR, capecitabine, methotrexate, raltitrexed and pemetrexed, or a combination thereof.

20. The method according to claim 18, wherein said thymidylate synthase mRNA is a human thymidylate synthase mRNA.
21. The method according to claim 20, wherein said antisense oligonucleotide comprises at least 7 consecutive nucleotides of the sequence as set forth in SEQ ID NO:1.
22. The method according to claim 18, wherein said antisense oligonucleotide comprises one or more phosphorothioate internucleotide linkages.
23. The method according to claim 18, wherein said antisense oligonucleotide comprises one or more 2'-O-methoxyethoxy modified sugars.
24. The method according to claim 18, wherein said neoplastic cells are *in vivo*.
25. The method according to claim 18, wherein said neoplastic cells are mesothelioma cells.
26. The method according to claim 25, wherein said mesothelioma cells are drug resistant.